REMARKS

Claims 1-10 remain in the application for further prosecution. Claim 1 has been amended to further distinguish the two Columbus references. Claim 8 has been amended to make clear that no process of use was intended and further to replace "blood anti-coagulant" with "reagents and/or filters", found at paragraph 0033 in the published application (or at page 9, line 18).

Rejections Under 35 U.S.C. § 102

Claims 1-3 and 8 have been rejected under 35 U.S.C. § 102(b) as anticipated by Columbus (U.S. 4,233,029). The Examiner has repeated verbatim his previous rejections and his response to arguments, excepting only updating the latter to refer to the amendment of September 9, 2005. There is no indication that the Applicants' specific analysis of Claim 1 had been considered, in which it was shown, element by element, why the Columbus structure should not be considered to anticipate the Applicants' device. If this had been a Final Rejection, an appeal would have been indicated. Since the current office action has been designated "non final", the Applicants have made further amendments to advance the prosecution and to avoid a final office action and the need for an appeal.

Columbus describes a device intended to provide controlled multidimensional flow with a predetermined peripheral configuration (see Claim 1). In other words, liquid added to the inlet port flows across the entire surface by capillary forces as directed by sets of grooves placed at an angle to each other. The present microfluidic device is clearly different, since an enclosed unidirectional capillary passageway connects the inlet port to an enclosed inlet chamber. Columbus teaches the opposite approach, as he directly states at column 6, lines 31-34, "the multidirectional flow achieved by the device as described is the overall flow occurring in two or more non-aligned directions as primarily distinguished from unidirectional flow."

Claim 1 will be compared with Columbus in the following newly revised table, in which the differences will be made clear.

Claim 1	Columbus
A microfluidic device for assaying a liquid biological sample of 20 μL or less comprising:	o Columbus may be considered a microfluidic device, although it uses drop volumes between 5 and 1000 μL (column

4, lines 45-47), which relate to the purpose of the Columbus device. That is, Columbus spreads his sample over the space between two surfaces, rather than filling an inlet chamber.

(a) an inlet port for receiving said sample;

- Columbus's "liquid access aperture 26" is an inlet port and <u>not</u> a capillary passageway, as the Examiner believes. Columbus requires that surfaces 16 and 18 are wetted, which permits them to transport the liquid sample by capillary action. The inlet port 26 is said to be sized to allow the sample drop to fill the port 26 and the space between the grooved surfaces 16 and 18 (column 4, lines 42-45). Fig. 2 shows a large drop placed on top of surface 24, which is drawn into the space between the two grooved surfaces by capillary action. If the port 26 is too small, both of the surfaces cannot be wetted by the continuous volume of the drop (column 4, lines 35-38). It is believed that Columbus means that a small opening would prevent liquid from exiting into the surfaces 16 and 18 by capillary forces acting at the exit of port 26. On the other hand, if the port is too large, the capillary forces would be negligible and liquid would flow onto the lower surface and not the upper surface (column 4, lines 38-42). In neither case is the liquid drop transported by capillary force along the sidewalls of inlet port 26.

- The problems associated with introducing liquid drops into the capillary space between the opposed surfaces are discussed extensively in his U.S. patents 4,254,083 and 4,439,526 (cited in the accompanying Information Disclosure Statement). Columbus provides dimensions which make it clear that the entry apertures have diameters much

	larger than the width of the capillary space, and also that the thickness of the surfaces is very thin compared to the diameter of the apertures. In effect, there is no passageway to provide capillary forces and it is the weight of the droplet that drives the liquid into the capillary space (see column 8, lines 17-20 of the '526 patent).
(b) an enclosed unidirectional capillary passageway in fluid communication with said inlet port;	o From the discussion opposite (a) above it should be clear that Columbus has no enclosed unidirectional capillary passageway. Instead he combines an inlet port with opposing grooved surfaces that spread a liquid drop in all directions.
(c) an enclosed inlet chamber in fluid communication at one side thereof with the enclosed unidirectional capillary passageway of (b);	o Columbus's space between surfaces 16 and 18 is not enclosed, since it must be open at the edges to allow air to be expelled (see column 6, lines 13-20). The flow of liquid is not unidirectional in Columbus, but multi-directional (column 6, lines 31-34). Furthermore, Columbus design requires entry at the middle of the space in order to uniformly distribute liquid in all possible directions, rather than from one side.
thereby providing said sample an entry into said enclosed inlet chamber;	o Columbus has an inlet chamber only insofar as it is a space, but not as an enclosed chamber, which requires that the liquid be confined within the chamber. Columbus indicates at column 10, lines 1-7 that the sample liquid can be distributed at the entire edge 20 or 22. Thus, Columbus's "chamber" does not correspond to the chamber disclosed by the Applicants.
said enclosed inlet chamber containing means for uniformly distributing said sample across said chamber;	o Columbus provides means for distributing liquid across his "chamber", but distributes it 360° from a central location and not from one side of the chamber to an opposite side. Columbus

should not be considered to distribute liquid unidirectionally, since he teaches that liquid flows along the grooves and jumps over the edges so that the liquid moves in all directions, depending on the orientation of the pair of grooves on any given devices. (see Figs. 4-6).

and (d) at least one vent passageway for removing air displaced by said liquid sample at a side opposite the entry of said capillary passageway.

- Columbus does not use a vent passageway, but merely allows air to be purged at all the four edges of his device. Air is not removed from a side opposite an entry of the liquid.

Columbus clearly intended that liquid added to his device would flow uniformly along the opposing grooves and in so doing force the air out from the space between the upper and lower surfaces, as is obvious from Fig. 1 and the discussion at column 6, lines 13-21. The Applicants' device introduces liquid through an enclosed passageway at one side of a closed chamber and forces air out through a vent located opposite the liquid inlet, and is therefore distinguished from the Columbus device.

However, the Examiner states that "Columbus anticipates an enclosed passageway. Walls 124 and 144 enclose passageway defined by 44b (see col. 11, lines 1-16; Fig. 10)." (Note that wall 144 appears only in Fig. 12, where it corresponds to wall 124 in Fig. 10). Figures 10 and 12 are quite different structurally, but they both suggest to the Examiner a closed passageway. However, with a closer review it will be seen that, in order to accomplish the uniform distribution of liquid essential to Columbus, a closed passageway is <u>not</u> created and that the liquid must fill the space between the two sets of grooves.

At column 11, lines 1-6, Columbus states that edge wall 124 is used to create a space between grooves 42b and 44b. Thus, the liquid can, and does, flow along both grooves to fill the

entire space, as is described in detail at column 5, line 1 to column 6, line 37. Columbus goes on to say that "Preferably, at least a portion of the space between grooves 42b and 44b is left exposed at edge surfaces by device 10, Fig. 9, whereby air can be vented or expelled as the menisci advance". Thus, expelling air at the periphery of the device is still provided. But, even if wall 124 were complete, air could still be expelled through the grooves 44, which are not enclosed by wall 124. Therefore, there is no enclosed passageway which enters a closed chamber and expels air from the side opposite the inlet. The purpose of the Columbus device is to create uniform flow multi-directionally between his opposing surfaces, which, as is discussed in column 1 is intended to overcome problems with earlier devices, such as trapping air and uncontrolled liquid flow.

Columbus also suggests using bridging studs between the opposed surfaces, which would provide space for venting air directly from grooves 42. He notes at column 11, lines 17-30 that uniform advancing liquid wave fronts are needed to provide a stable bias potential. Further, at lines 31-36, referring to Fig. 11, Columbus states his preference for the flow along grooves 42 to fill the entire width from 20b to 20b before the flow along grooves 44b results in the wave fronts meeting at 134. Again, this means that air must be expelled all along edges 20b.

Wall 144 appears only in Example 2 as part of Fig. 12. It appears to be continuous since it seems to direct liquid around corners 140, 142, and 144 into isolated test areas 136 and 138. However, if these test areas are to be filled uniformly from grooves from the upper grooves, then air must be expelled from the opposing bottom grooves as in Fig. 10. Thus, the upper grooves do not provide a closed passageway that ends in a closed chamber, as in the Applicants' device where air inherently is moved ahead of liquid passing through the passageway and expelled,

along with air in the closed chamber, at a vent from the chamber at a side opposite the entry point.

That the Examiner gives unduly broad reading of the Applicant's claims also may be seen by considering whether they would be infringed by Columbus's device.

Claim 1	Columbus
o A microfluidic device for assaying a liquid biological sample of 20 μL or less comprising:	o If Columbus's device is assumed to employ much more than 20 μL typically, it would arguably <u>not</u> infringe.
o An inlet port for receiving said sample	o Columbus does have an inlet port 26 and would infringe this element of the claim.
o an enclosed unidirectional capillary passageway in fluid communication with said inlet port;	o Columbus's opening 26, if considered an inlet port, would be contended to <u>not</u> be a capillary passageway, since at most one would have to consider the thickness of surfaces 12 to be a capillary passageway. Furthermore, as discussed above it is likely that a sample drop will be pulled through the opposing grooved surfaces by capillary forces, while inlet port 26 is too large to contribute capillary forces.
o an enclosed inlet chamber in fluid communication at one side thereof with the enclosed unidirectional capillary passageway of (b) thereby providing said sample an entry into said enclosed inlet chamber.	o Columbus would contend that his open-sided device was not an enclosed inlet chamber, nor did the space between his opposing surfaces receive fluid at one side from his inlet 26.
o said enclosed inlet chamber containing means for uniformly distributing said sample across said chamber;	o Columbus would point out that his inlet 26 is centrally located and not from one side, so that liquid is distributed in all directions.
o and (d) at least one vent passageway for removing air displaced by said liquid sample at a side opposite the entry of said capillary passageway.	Columbus would contend that his purging of air at all four edges of his device could not be considered a vent passageway or four vent passageways. In particular, that by opposing grooved surfaces, air is moved all directions at once. Its flow is not directed to a side opposite the liquid entry.

The Examiner considers that, in Claim 8, blood anti-coagulant is deposited in the inlet chamber to be a process or intended use limitation. Applicants disagree with his interpretation, but have amended Claim 8 above to avoid such an anticipation. Further, they have replaced "blood anti-coagulant" with the more general "reagents and/or filters," which is also supported by the specification.

Claims 1-3 and 8-10 have been rejected also under 35 U.S.C. 102(b) as anticipated by Columbus, U.S. 4,618,476. Columbus's '476 device is significantly different from his '029 device. He considered it to be an improvement, in which barriers and slots replace the opposed grooves found in the '029 patent. In this device, when two different liquids enter separate openings and move toward each other, the capillary transport zone is sealed at the edges and air is expelled from apertures 60 and 62 (Fig. 5, column 4, lines 53-57). This is also seen more clearly in Fig. 8 (column 5, lines 39-50) where two different liquids enter at two apertures 140 and 142 and meet at the center. Air is released from a series of holes 60, 62.

The Examiner referred particularly to Fig. 16, described at column 7, lines 15-38, which is a device intended to allow two liquids to flow side-by-side without mixing. The liquids are introduced separately through inlet ports 410 and travel along the right and left sides of transport zone 30g. The ribs are <u>not</u> used just to distribute liquids across the chamber, as the Examiner states, but are used to remove air from the transport zone (see column 4, lines 1-5 and 29-33). Columbus brings the two liquids in contact with ion-selective electrodes (ISE) disposed along the passage through which the liquids pass. Columbus sums up at column 7, beginning at line 60 "As a result, two dissimilar but misible liquids introduced into zone 30g via apertures 410 will flow side-by-side, along serpentine paths, producing a junction that approximately bisects apertures 42C and is substantially free of convection mixing. Portions of each liquid, one of

which is a reference liquid, are withdrawn through apertures into contact with their respective ISE's, ..."

Claim 1 will be compared with Columbus '476 in the following table, in which the differences will be made clear.

Claim 1	Columbus '476
A microfluidic device for assaying a liquid biological sample of 20 μL or less comprising:	o Fig. 16 discloses a device for handling <u>two</u> liquids flowing concurrently through the device <u>without</u> <u>mixing</u> (column 7-8). Fig. 8 discloses a device for handling <u>two</u> liquids that flow toward each other.
(a) an inlet for receiving said sample	o Fig. 16 contains <u>two</u> apertures (410) for two samples <u>not</u> one inlet for one sample. Fig. 8 contains <u>two</u> apertures 140 and 142 for introducing separate liquids.
(b) an enclosed unidirectional capillary passageway in fluid communication with said inlet port;	o Consistent with the two apertures (410), . Fig. 16 shows <u>two</u> passageways in fluid communication with the inlet apparatus. Also true of the embodiments of Fig. 8.
(c) an enclosed inlet chamber in fluid communication at one side thereof with the enclosed unidirectional capillary passageway of (b);	o Capillary transport zone 30g maintains concurrent flow of <u>two</u> liquids, that flow out through slots 450 to their respective ion-selective electrodes. Thus, rather than providing uniform distribution of the two liquids across the transport zone 30g. They are kept separate. The transport zones of Columbus are <u>not</u> enclosed inlet chambers to which liquids enter from capillary passageways. Instead they are capillary passageways entered from apertures and from which air is expelled at multiple exit holes.
thereby providing said sample an entry into said enclosed inlet chamber;	o As noted above, the flow of <u>two</u> liquids are concurrent or opposed and not mixed. The objective of the design of the device in Fig. 16 is to deliver the liquids to their respective ion-selective electrodes through slots 450. In Fig. 8, the liquids meet midway between the entry ports.

said enclosed inlet chamber containing means for uniformly distributing said sample across said chamber;	o In Fig. 16, the flow of two liquids, which are kept separate, are not distributed uniformly across the transport zone 30g. Where air is purged in Fig. 16 is not clear. In Fig. 8 it appears that air is purged through vents at the top of the transport zone, but in Fig. 16 those vents are not mentioned. The only air vent mentioned is 480 at the end of a waste chamber 470.
and (d) at least one vent passageway for removing air displaced by said liquid sample at a side opposite the entry of said capillary passageway.	o The vent in the Applicant's chamber is opposite the entry of their inlet chamber. The only vent identified in Fig. 16 is 480 at the end of waste chamber 470, <u>not</u> in the transport zone 30g. Fig. 8 uses multiple vent openings.

Claim 8 has again been considered a process or intended use limitation. As discussed above, the Applicants have amended Claim 8 to clarify their intent.

<u>Rejections Under 35 U.S.C. § 103</u>

Claims 4-6 have been rejected under 35 U.S.C. 103(a) as unpatentable (i.e. obvious) over Columbus '029 in view of Peters, U.S. 6,296,126 B1, the later cited for the use of wedge-shaped cut-out structures. Peters is a co-inventor in the present application, and his patent was cited in paragraph 0037 of the published application (or page 11, line 17). Claims 4-6 are dependent from Claim 1 and if, as the Applicants contend, Claim 1 is distinguished from Columbus and patentable, then Claims 4-6 should also be allowable. Futhermore, Peters does not disclose his posts to distribute liquid uniformly in parallel to the posts, but instead uses the v-shaped grooves as channels for the liquid.

Claim 7 has been rejected under 35 U.S.C. 103(a) as unpatentable over Columbus '029 in view of Bedingham et al, U.S. 6,734,401 B2, cited for disclosing a tapered inlet port to engage a

pipette tip. As with Claims 4-6, Claim 7 should be allowable if Claim 1 is patentable over Columbus.

In view of the above remarks the Examiner is urged to allow the amended claims remaining in the application. If further amendments are believed necessary, the Examiner is invited to contact the Applicant's attorney at the telephone number provided below.

Respectfully submitted,

2/28/06
Date

Harold N. Wells

Harold N. Wells; Reg. No. 26,044
Kelley Drye & Warren LLP
333 West Wacker Drive
Suite 2600
Chicago, IL 60606
Attorney for Applicants
Tel.: (312) 857-2336